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## Case Report

## Pulmonary adenocarcinoma masquerading as diffuse inflammatory interstitial lung disease ☆☆☆☆☆

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## ABSTRACT

Pulmonary adenocarcinoma has long intrigued both internists and pulmonologists because it seems to have unique epidemiologic, pathologic and clinical features. We report a case of multifocal well-differentiated adenocarcinoma, mimicking honeycombing and diffuse inflammatory interstitial lung disease.

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## 1. Introduction

Pulmonary adenocarcinoma has long intrigued both internists and pulmonologists because it seems to have unique epidemiologic, pathologic and clinical features. We report a case of multifocal well-differentiated adenocarcinoma, mimicking honeycombing and diffuse inflammatory interstitial lung disease.

## 2. Case: A

52 year old Hispanic non smoker male with no past medical history presented with persistent dry cough, occasional fever and dyspnea at rest. The symptoms were gradual in onset and progressively worsening for about 6 months with no hemoptysis, night sweats or pleuritic chest pain. Patient admitted to have been treated with multiple antibiotics by his primary care giver, but without any improvement in the symptoms. He also had an x-ray and the Computed Tomography (CT) of the chest 3 months back which showed diffuse interstitial changes in both the lungs. Pulmonary function test showed a restrictive pattern. Patient had also received trials of bronchodilators and steroids with no improvement. On admission, patient looked dyspneic with

respiratory rate of 24/min and pulse of 110. Pulse oxymeter showed the saturation of 84% on room air and 95% on 100% non re-breather mask. Examination of chest revealed bilateral diffuse fine crackles. Other systemic examinations were normal. Chest x-ray showed diffuse interstitial changes and CT chest showed diffuse distortion of lung parenchyma with ground glass opacity, honeycombing and cystic changes. Patient was started on steroids, bronchodilators and broad-spectrum antibiotics. Initial complete blood count, metabolic profile, Anti-Nuclear Antibody (ANA), Rheumatoid Factor (RF), Angiotensin Converting Enzyme (ACE) and alpha-1-antitrypsin levels were normal. Multiple sputum samples for gram stain and cultures for bacteria including mycobacterium tuberculosis were normal. Fiber optic bronchoscopy with bronchial lavage (BAL) and transbronchial biopsy (TBB) was done. Pathological examination of the biopsy showed well-differentiated adenocarcinoma with mixed bronchoalveolar pattern. Bone scan showed sclerotic thoracolumbar vertebral metastases. Patient was started on chemotherapy for unresectable stage IV adenocarcinoma.

## 3. Discussion

Because of the unique radiographic features of Bronchoalveolar Carcinoma (BAC) it is often called the “masquerader”. Bronchoalveolar carcinoma may classically manifest as an interstitial lung disease on chest radiograph, it may produce extensive diffuse pulmonary infiltrates that can mimic those with infectious etiologies.<sup>1</sup> Its presentation may be confused with pneumonia or other inflammatory conditions in the lung, and only after a patient fails to improve a course of antibiotics or corticosteroids does one entertain the diagnosis of pulmonary adenocarcinoma.

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In our case, patient presented with cough and progressive shortness of breath. CT of the chest showed diffuse and extensive cystic changes, with ground glass opacities, honeycombing and distortion of normal lung parenchyma in both the lungs. Hazy consolidations were seen at both the lung bases representing acute process. Patient had failed antibiotic therapy and corticosteroid therapy multiple times. The differential diagnosis of these findings included cryptogenic organizing pneumonia, chronic eosinophilic pneumonia, hypersensitivity pneumonitis, drug induced pneumonitis and usual interstitial pneumonia (UIP). But all these possibilities were ruled out by the absence of hyper-eosinophilia in the blood and BAL fluid, absence of response to corticosteroid and absence of response to antibiotics. Also, patient denied using any drug or any recent treatment apart from antibiotics and corticosteroids. Patient also denied any significant occupational exposure. Initially, BAC was not thought to be the cause of this radiographic appearance because pulmonary architectural is usually preserved in this condition. Finally, the progression of the disease process with clinical and radiological deterioration led us to suspect underlying malignant process. The histopathological specimen obtained from transbronchial biopsy revealed well-differentiated bronchoalveolar carcinoma along with inflammatory fibrosis and honeycombing.

The World Health Organization classifies lung adenocarcinomas into acinar, papillary, bronchoalveolar, and mucus-secreting.<sup>2</sup> But this histopathological variant has not been described by the latest World Health Organization (WHO) classification of lung tumors although rare cases have been reported.<sup>3</sup> The exact pathogenesis of this phenomenon is under study but seems prominent inflammation and fibrosis overshadows tumoral proliferation and masquerade as a benign reactive process. This can confuse the physician and can be mistaken as benign inflammatory lungs disease and delay the diagnosis.<sup>4</sup> On the contrary, the association of lung cancer in pre-existing interstitial lung disease has been well documented. Patient with UIP and pulmonary fibrosis in relation with collagen vascular and occupational lung diseases can develop lung carcinoma years after the diagnosis of ILD is established.<sup>5,6</sup>



**Fig. 1.** CT chest: showing diffuse and extensive cystic changes, with ground glass opacities, honeycombing and distortion of normal lung parenchyma in both the lungs.



**Fig. 2.** CT chest: Hazy consolidations are seen at both the lung bases representing acute process.

Bronchoalveolar carcinoma is a distinct clinicopathologic entity and a subtype of adenocarcinoma that appears to arise from type II pneumocytes and may manifest radiologically as a solitary peripheral nodule (SPN), multifocal disease, or a rapidly progressing pneumonic form, which can spread rapidly from one lobe to another. It usually is located peripherally; the cytology is well-differentiated and grows along intact alveolar septa (the so-called “lepidic” growth pattern) but without evidence of vascular or pleural involvement, and tendency for both aerogenous and lymphatic spread. Histologically, it is divided into 3 subtypes: mucinous, nonmucinous and mixed (Figs. 1 and 2).

Clinically, patients may be either symptomatic (usually the ones that have SPN) or may present with cough and shortness of breath. Cough may be nonproductive or may be associated with large amounts of sputum, which is termed as “bronchorrhea” (usually occurs in the mucinous histological subtype).<sup>7</sup>

The diagnosis of BAC requires examination of the entire tumor after resection. Transbronchial biopsy should be not relied upon since BAC is a non-invasive tumor and diagnosis is dependent upon demonstration of lepidic growth without invasion of other structures.<sup>8</sup> So even if transbronchial biopsy shows BAC growth pattern, this does not confirm the diagnosis. However, like in our case, if BAC presents radiologically with a ground glass appearance or as an infiltrate and the biopsy demonstrated the BAC growth pattern the diagnosis of BAC may be confirmed, as non BAC adenocarcinoma does not present as ground glass.<sup>8</sup>

Treatment depends on the disease stage and extent and may include surgical resection for the localized form or radiation therapy with or without chemotherapy in unresectable cases.<sup>9</sup> BAC with epidermal growth factor receptor (EGFR) gene mutation may benefit from tyrosine kinase inhibitor.<sup>10</sup>

#### 4. Conclusion

Bronchoalveolar adenocarcinoma should be kept in the differential diagnosis of any patient presenting with interstitial lung disease with architectural distortion, particularly if it is not responding to antibiotics and corticosteroid therapy. This case

highlights the difficulties faced in the diagnosis of pulmonary adenocarcinoma in presence of inflammation and fibrosis. It also reinforces the importance of tissue diagnosis in patients with Interstitial Lung Disease.

### Conflict of interest statement

Neither the author nor any of the co-author has any financial or personal relationships with other people or organizations that could inappropriately influence (bias) our work.

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